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TECH CENTER 1600/2900

PATENT

ATTORNEY DOCKET NO.: REGEN1500-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Vale et al. Art Unit: 1641  
Application No.: 09/502,664 Examiner: K. Padmanabhan  
Filed: February 11, 2000  
Title: METHOD OF AFFINITY PURIFYING PROTEINS USING MODIFIED  
BIARSENICAL FLUORESCIN

Box Non-Fee Amendment  
Commissioner for Patents  
Washington, D.C. 20231

TRANSMITTAL SHEET

Sir:

Transmitted herewith for the above-identified application please find:

1. Response to the Office Action dated July 24, 2001;
2. Return Receipt Postcard.

| CERTIFICATION UNDER 37 CFR §1.8   |                           |
|---|---------------------------|
| I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, August 22, 2001, in an envelope addressed to:<br>Commissioner for Patents, Washington, D.C. 20231. |                           |
| Aldon Griffis<br>(Name of Person Mailing Paper)   |                           |
| Aldon Griffis<br>(Signature)  | August 22, 2001<br>(Date) |

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Filed: February 11, 2000  
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The Fee for this Response is calculated as follows:

| For                   | Claims Remaining<br>After Amendment | Highest Number<br>Previously Paid For | Extra<br>Claims | Large Entity<br>Rate | Small Entity Rate | Calculations |
|-----------------------|-------------------------------------|---------------------------------------|-----------------|----------------------|-------------------|--------------|
| Total Claims          | 103                                 | 103 (20)                              | 83              | x \$18               | x \$09            | \$ .00       |
| Independent<br>Claims | 8                                   | 8 (3)                                 | 5               | x \$80               | x \$40            | \$ .00       |
| Multiple Claims       |                                     |                                       |                 | \$270                | \$135             | \$ .00       |
| Basic Filing Fee      |                                     |                                       |                 | \$710                | \$355             | \$ .00       |
|                       |                                     |                                       |                 |                      | TOTAL FEE         | \$ .00       |

No fee is deemed necessary in connection with the filing of this paper. However, if a fee is required, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 50-1355. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

Date: August 22, 2001



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AUG 28 2001

TECH CENTER 1600/2900 PATENT  
Attorney Docket No.: REGEN1500-11

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Vale et al. Art Unit: 1641  
Application No.: 09/502,664 Examiner K. Padmanabhan  
Filed: February 11, 2000  
Title: METHOD OF AFFINITY PURIFYING PROTEINS USING  
MODIFIED BIARSENICAL FLUORESCIEIN

Box Non-Fee Amendment  
Commissioner for Patents  
Washington, D.C. 20231

**RESPONSE TO THE RESTRICTION REQUIREMENT**

Sir:

Responsive to the Restriction Requirement mailed July 24, 2001 (Paper No. 6), in connection with the above-identified patent application, consideration of the following remarks is respectfully requested.

Pursuant to the restriction requirement, Applicants elect with traverse the claims of Group I, claims 1 to 12, directed to methods of isolating a polypeptide, which is modified to contain a fluorescein arsenical helix (FIAsH) target sequence. In addition, pursuant to the request to elect a species of solid support, Applicants elect with traverse the species "agarose."

**A. Regarding the Restriction Requirement**

The restriction requirement is traversed with respect to the division of Groups I, IV, V, VII and VIII from each other. The restriction requirement also is traversed with respect to the division of Groups II and III from each other.

**CERTIFICATION UNDER 37 CFR §1.8**

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, August 13, 2001, in an envelope addressed to:  
Commissioner for Patents, Washington, D.C. 20231

*Aldon Griffis*  
Aldon Griffis

August 22, 2001

**1. Regarding Groups I, IV, V, VII and VIII**

The claims of elected Group I and Groups IV, V, VII and VIII all are directed to methods of isolating a polypeptide, which is modified to contain a FIASH target sequence motif, at least by binding the polypeptide to a FIASH binder compound, which is immobilized to a solid support. It is stated in the Office Action that the claims of the various Groups differ from each other in the steps involved and/or the structure of the polypeptides.

With respect to the structures of the polypeptides, however, Applicants point out that the polypeptides to be isolated differ only in whether the polypeptide has been modified such that the FIASH target sequence is positioned at the C-terminus (Groups IV and VII) or at the N-terminus (Groups V and VIII). Applicants submit that there would be no apparent reason why, for example, a search of one of a polypeptide modified at the C-terminus would be different from a search for a polypeptide modified at the N-terminus, and there is no indication in the Office Action of such a reason. Further in this respect, it is noted that the claims of elected Group I do not recite a position for the FIASH target sequence and, therefore, the subject matter of the elected claims can encompass the FIASH target sequence modified polypeptides in any or all of Groups IV, V, VII and VII. As such, while the claims of Groups I, IV, V, VII and VIII are directed to subject matter that is independent and patentably distinct, it is submitted that the position of the FIASH target sequence with respect to a terminus of a polypeptide to be isolated is not a sufficient basis for dividing, for example, the claims of Group IV from those of Group V, or the claims of Group VII from those of Group VIII; for dividing the claims of Groups IV and VII (FIASH target sequence at C-terminus) from those of Groups V and VIII (FIASH target sequence at N-terminus); or for dividing any of those claims from the claims of elected Group I (position of FIASH target sequence not specified).

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With respect to the steps recited in the claims of Groups I, IV, V, VII and VIII, Applicants point out that steps c) and d) of claims 38 (Group IV) and 77 (Group VII) correspond to steps a) and b) of claims 46 (Group V) and 88 (Group VIII) and, similarly, steps a) and b) of claims 38 and 77 correspond to steps c) and d) of claims 46 and 88). As such, the steps required in the claims of the various Groups are substantially similar, and merely are performed in a different order. Applicants submit that there would be no apparent reason why, for example, a search of the methods of any of these Groups would be different from a search for a method of any of the other Groups, and there is no indication in the Office Action of such a reason. Further in this regard, it is noted that steps a) and b) of claim 1 (elected Group I) encompass the subject matter of steps a) and b) of claims 46 and 88 and steps c) and d) of claims 38 and 77. As such, while the claims of Groups I, IV, V, VII and VIII are directed to subject matter that is independent and patentably distinct, it is submitted that the steps to be performed to practice the claimed methods and the order of the steps is not a sufficient basis for dividing, for example, the claims of Group IV from those of Group V, or the claims of Group VII from those of Group VIII; for dividing the claims of Groups IV and VIII (affinity purification based on tag, followed by FAsH-based purification) from those of Groups V and VIII (FAsH-based purification, followed by purification based on tag); or for dividing any of those claims from the claims of elected Group I (comprising FAsH-based purification).

In summary, the claims of Groups I, IV, V, VII and VIII, while independent and patentably distinct, are directed to methods for isolating a polypeptide that contains a FAsH target sequence, which can be at any position (Group I), including, for example, at the N-terminus (Groups V and VIII) or C-terminus (Groups IV and VII), wherein the methods comprise a step of binding the polypeptides to a FAsH compound immobilized on a solid support. As such, the claimed subject matter is so closely related that it would not appear to present an undue burden on the Examiner or the U.S. Patent and Trademark Office to examine the claims of Groups I, IV, V, VII and VIII together, and no objective reason is set forth in the Office Action to indicate why a search of any one of the Groups would be different from a search of any of the other Groups. Accordingly, it is

respectfully requested that these claims of Groups IV, V, VII and VIII be rejoined and examined together with the claims of elected Group I (claims 1 to 12).

## **2. Regarding Groups II and III**

With respect to Groups II and III, it is noted that each of the Groups contains claims directed to a DNA construct (e.g., claim 13 of Group II, and claim 24 of Group III), as well as to a method of using the DNA construct (e.g., claim 35 of Group II, and claim 74 of Group III). The basis for dividing the claims as set forth in the Office Action is that the DNA constructs differ in their 3' and 5' ends. Applicants point out, however, that the 3' end of the DNA construct of claim 13 (Group II), for example, corresponds to the 5' end of the DNA construct of claim 24 (Group III), i.e., encodes a FIASH target sequence, and, similarly, the 5' end of the DNA construct of claim 13 corresponds to the 3' end of the DNA construct of claim 24, i.e., encodes an affinity tag. There is no objective reason set forth in the Office Action as to why the different orientation of the ends of the construct would require separate searches to be performed, and it would not appear that such a difference is sufficient to divide the claims into separate Groups. It is noted that the different classification of the Groups appears to be based on the method claims, although there is no discussion of this in the Office Action. Accordingly, it is respectfully requested that the claims of Groups II and III be rejoined or, in the alternative, that at least claims 13 to 23 of Group II and claims 24 to 34 of Group III, each of which is directed to a DNA construct, be rejoined into a single Group.

**B. Regarding the Species Election**

It is requested in the Office Action that a species of solid support from among the solid supports recited in claims 8, 41, 50, 62, 67, 83, and 92 be elected, depending on the election pursuant to the restriction requirement. There is no reason set forth in the Office Action for requiring such an election or to support the request to elect a species.

Applicants traverse the request to elect a species because, while the species as set forth are independent and patentably distinct, the various solid supports share a commonality of operation, function and effect with respect to the present invention (MPEP § 806.04(e)). Specifically, the solid supports merely are used as a medium to contain a FLaSH binding compound, for example, in a chromatography method.

Since the various solid supports have a commonality of operation, function and effect, it is submitted that an election of one species should not be required and that use of all of the solid supports in the methods of the invention should be examined together.

In summary, the claims of Group I, claims 1 to 12, and the species "agarose" are elected with traverse. With respect to the restriction requirement, it is respectfully requested that the Examiner rejoin the claims of Groups IV, V, VII and VIII with those of elected Group I and examine all of the claims together, and that the Examiner further rejoin the claims of Groups II and III together, particularly with respect to the claims directed to DNA constructs. With respect to the species election, it is respectfully requested that the Examiner rejoin and examine all of the solid supports.

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No fee is deemed necessary in connection with the filing of this Response. However, if any fee is required, the Commissioner is authorized to charge any fee (or credit any overpayment) to Deposit Acct. No. 50-1355.

The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Respectfully submitted,

Dated: August 22, 2001



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